DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

I-009332-D-0093

JUN 25 2007

U.S. Department of the Interior
Fish and Wildlife Service
Aquatic Animal Drug Approval Partnership Program
Attention: David Erdahl, Ph.D.
Branch Chief, AADAP
4050 Bridger Canyon Road
Bozeman, MT 59715

Re: Request for amended authorization for oxytetracycline medicated feed

Dear Dr. Erdahl:

You are authorized to slaughter 100 million fish to (1) market for human food use the edible tissues derived from experimental animals or (2) release into public waters for possible human consumption experimental animals treated as described in this letter. The use of oxytetracycline dihydrate administered as a medicated feed as described in your April 3, 2007, submission is consistent with the public health.

AMENDED AUTHORIZATION

DRUG	TERRAMYCIN 200 for Fish
Dosage Form	Type A medicated feed
Route of Administration	Oral
SPECIES	Fish as described in Appendixes VIa and VIb
Class	All life stages
Number of Animals	100 million
MAXIMUM DOSE (or Range) Frequency and Duration	Objective A – Salmonids fed medicated feed containing 2.5 to 3.75 g oxytetracycline/ 100 lb of fish per day for 10 days at water temperatures greater than 9 °C are included in the oxytetracycline approval under 21 CFR 558.450(d)(2)(ii). Objective B – Salmonids fed medicated feed containing 2.5 to 3.75 g oxytetracycline/ 100 lb of fish per day for 10 days at water temperatures between 4 and 9 °C. Objective C – Salmonids fed medicated feed containing 10 g oxytetracycline per 100 lb of fish per day for 14 days in water temperatures not below 4 °C.

	Objective D –Cool and warmwater fish species fed medicated feed containing 2.5 to 3.75 g oxytetracycline/100 lb of fish per day for 10 days at water temperatures between 9 and 17 °C. Objective E – Abalone fed up to 6 g oxytetracycline per 100 lb body weight per day for 14 days. Objective F - Salmonids fed at either the approved drug level (2.5-3.75 g oxytetracycline) or at 10.0 g oxytetracycline per 100 lb of fish per day for 14 days.
MINIMUM WITHDRAWAL PERIOD	Objective A – 21 days. No withdrawal period is required for fish that will not be catchable for 21 or more days after release, or are illegal for harvest. Objective B –21 days. No withdrawal period is required for fish that will not be catchable for 21 or more days after release, or are illegal for harvest. Objective C –70 days. No withdrawal period is required for fish that will not be catchable for 70 or more days after release, or are illegal for harvest. Objective D – 40 days. No withdrawal period is required for fish that will not be catchable for 40 or more days after release, or are illegal for harvest. Objective E – 35 days. No withdrawal time is required for abalone that will not be harvestable for 35 or more days after release, or are illegal for harvest. Objective F – 21 days for fish fed at the approved level. No withdrawal period is required for fish fed at the approved dose that will not be catchable for 21 or more days after release or are illegal for harvest. 70 days for fish fed at the high dose (10 g OTC). No withdrawal period is required for fish that will not be catchable for 70 or more days after release or are illegal for harvest.

COMMENTS	The investigational withdrawal periods may be incorporated into grow-out periods for the treated fish.
RENDERING	Fish may be rendered at any time.
REFERENCE TO OTHER AUTHORIZATIONS	All previous authorizations are superseded.

Clinical investigations for this INAD cover only the treatment regimen stated above. The combining of this treatment with any other drug will require a separate authorization. Drugs given to control animals must be administered in full compliance with the currently approved use. Your investigators should be made aware of their responsibilities under sections 511.1(b)(7)(ii) and 511.1(c)(1) of the new animal drug regulations.

Clinical tests conducted under the provisions of this letter do not exempt investigational animals and their products from compliance with any other applicable inspection requirements.

In order for us to complete our files, the disposition of all investigational animals and unused drug must be reported to this office, as well as adverse reactions observed. Please refer to this letter by date and INAD number when reporting the details of clinical investigations or the disposition of investigational animals.

ENVIRONMENTAL CONSIDERATIONS

The investigational use of TERRAMYCIN 200 for Fish (oxytetracycline dihydrate) in fish continues to fall within the categorical exclusion in 21 CFR 25.33(e). Therefore, neither an environmental assessment (EA) nor an environmental impact statement is required. A categorical exclusion from preparation of an EA and an environmental impact statement does not relieve you of the responsibility for determining and meeting all Federal, State, and local environmental and occupational laws and regulations that apply to the manufacturing, use, and disposal of the investigational drug.

You are responsible for complying with the Federal Clean Water Act as implemented under the National Pollutant Discharge Elimination System (NPDES), as well as any applicable ground-water pollution requirements, for all investigational sites covered under this INAD. You must contact the offices responsible for issuing NPDES permits, and other similar permits, to be certain they have no objection to the use and release of the investigational drug.

Please notify CVM if the scope of your investigation changes (e.g., if additional facilities will treat fish, and/or if the protocol changes in ways that could result in increased environmental exposure, etc.).

INVESTIGATIONAL LABELING

We remind you that the investigational new animal drug must be manufactured, processed, packaged, and labeled in such a way as to maintain appropriate standards of identity,

strength, quality, and purity as needed for safety and to give significance to investigations made with the drug.

The investigational labeling, as provided in your April 3, 2007, submission, should be affixed to your investigational drug product prior to shipment for studies conducted under 21 CFR 511.1(a) or (b), as appropriate. The investigational labeling should be affixed to each individual drug container.

SHIPMENT AND DELIVERY NOTIFICATION

The new animal drug regulations, sections 511.1(b)(3) and (4) require the sponsor to submit specific information prior to each shipment or other delivery of the drug for clinical investigation in animals. The agency has devised a form (Form FDA 3458), which you as the sponsor may use to report shipments for clinical trials. You may file the notice of the drug shipment electronically to CVM. Please refer to the Center's electronic submission information on the CVM website at http://www.fda.gov/cvm/esubstoc.html.

You must maintain records of dates, amount of drug received in each shipment, and batch or code mark of each shipment for a period of 2 years after such shipment and delivery. These records should be made available for inspection and copying upon our request.

COUNTING NUMBERS OF FISH

You should note that this authorization is for a specific number of fish. You should begin counting the number of animals used from the date you receive our letter starting at zero. Previous authorizations are superseded. In the future, it would be helpful if you would supply the total number of animals used along with your annual reports.

Having a specific number of animals, rather than annual numbers, facilitates our tracking of fish numbers under the INAD. We remind you that a fish treated more than once still only counts as a single animal toward the authorization.

Additional numbers of animals may be requested in the future. A request for additional animals should be made with sufficient lead time to allow us to process an amended authorization.

ANNUAL REPORTS

We remind you of the continued necessity to provide annual reports under the FDA/CVM Aquaculture Workload Plan. Your annual report should comprise: a) a brief summary of the past year's activities and accomplishments in each of the technical sections for the NADA; b) certification of accountability of all drugs shipped under the INAD, records maintenance for FDA inspection, compliance with the provisions of 21 CFR Part 511, including notification of adverse effects relative to humans, target animals, or the environment resulting from the use of the investigational drug; c) a list of all investigators, facilities, and species treated; and d) a copy of the current study protocol(s) noting any modification or revision. We recommend that any changes to pivotal study protocols be reviewed by CVM prior to initiating further investigations.

PROTOCOL COMMENTS

The revised protocol is adequate for the development of supportive effectiveness data and to provide additional target animal safety data. The protocol does contain a few minor errors that should be corrected prior to delivering the protocol to investigators.

1. Multiple sections of the protocol refer to investigators preparing medicated feed by top-coating feed with the TERRAMYCIN 200 for Fish Type A medicated article product. The approved method for preparing medicated feed is by incorporation prior to pelleting. The top-coating method may be used when necessary for investigations conducted under the INAD. However, you should contact Phibro Animal Health regarding a development plan for the data necessary to add the top-coating preparation method to the label. If you or Phibro elect not to pursue the approval of the top-coating as a method to prepare medicated feed, the top-coating preparation instructions should be removed from the protocol.

2. Sections IX (Pathogen/disease consideration-Section C), X (Section B), and XII (Section 1) refer to parasite, parasite infestation, and parasite load, respectively. Because the investigational drug, oxytetracycline dihydrate, is an antimicrobial, those sections of the protocol should refer to bacterial pathogens. If the statement including the reference to a parasitic infestation is not appropriate when referring to a bacterial disease, the statement should be removed.

3. Form OTC-1 includes the date of the previous authorization. With the granting of this authorization, the date of the CVM authorization letter will need to be changed to the date of the letter sent in response to this submission.

4. Form OTC-2a includes the term Medicated Feed Article. This form appears to be a form on which to record use of TERRAMYCIN 200 for Fish Type A Medicated Article. The protocol does refer to the Type A medicated article correctly. Therefore, the form should be revised with "Type A medicated article" replacing "Medicated Feed Article."

If you submit correspondence relating to this letter, you should reference this letter by date and the principal submission identifier found at the top of this letter. If you have any questions or comments, please contact Dr. Joan C. Gotthardt, Director, Division of Therapeutic Drugs for Food Animals, at 301-827-7571.

Sincerely,

Steven D. Vaughn, DVM
Director
Office of New Animal Drug Evaluation
Center for Veterinary Medicine